

**WHAT IS CLAIMED IS:**

1. An HCV protease comprised of an amino acid sequence in which amino acid at at least one of positions 155, 156 or 168 of the native HCV NS3 protease is mutated.
2. The HCV protease according to claim 1, wherein said sequence comprises a mutation at at least one of positions 155 or 156 of the native HCV NS3 protease.
3. The HCV NS3 protease according to claim 2, wherein amino acid at position 155 is replaced with a non-arginine amino acid
4. The HCV NS3 protease according to claim 2, wherein amino acid at position 156 is replaced with a non-alanine amino acid.
5. The HCV NS3 protease according to claim 1, wherein amino acid at position 168 is replaced with an amino acid other than: aspartic acid, glutamic acid and glutamine.
6. An HCV NS3 protease comprised of an amino acid sequence defined by SEQ ID No.2, comprising one or more mutations selected from the group consisting of: R155Q; R155W; A156G; A156T; A156V; D168A; D168G; D168H; D168N; and D168V.
7. The HCV NS3 protease according to claim 6, further comprising one or more mutations selected from the group consisting of: Q80R; and S122R.
8. The HCV NS3 protease according to claim 6 or 7, further comprising one or more mutations selected from the group consisting of: S20N; R26K; Q28R; A39T; Q41R; I71V; Q86R; P89L; P89S; S101N; A111S; P115S; L144F; A150V; V158L; E176K; and T178S; M179I; M179V and M179T.
9. An HCV NS3 protease comprised of 90% identity with amino acid sequence defined by SEQ ID No.2, further comprising one or more mutations selected from the group consisting of: R155Q; R155W; A156G; A156T; A156V; D168A; D168G; D168H; D168N; and D168V.
10. The HCV NS3 protease according to claim 9, further comprising one or more mutations selected from the group consisting of: Q80R; and S122R.
11. The HCV NS3 protease according to claim 9 or 10, further comprising one or more mutations selected from the group consisting of: S20N; R26K; Q28R; A39T;

Q41R; I71V; Q86R; P89L; P89S; S101N; A111S; P115S; L144F; A150V; V158L; E176K; and T178S; M179I; M179V and M179T.

12. A recombinant nucleic acid encoding an inhibitor-resistant HCV NS3 protease according to anyone of claim 1.
13. A nucleotide probe capable of hybridizing under stringent conditions to a nucleic acid sequence as defined to claim 12.
14. A vector incorporating a nucleic acid as defined in claim 12.
15. A host cell transfected with the vector as defined in claim 14.
16. A method for evaluating HCV NS3 protease activity of inhibitor-resistant NS3 protease, said method comprising the steps of:
  - incubating host cells as defined in claim 15 under conditions which cause said protease to be expressed; and
  - measuring the replication of said nucleic acid;

wherein the level of replication of said nucleic acid is proportional to the activity of said expressed protease.

17. A method for identifying potential a second generation inhibitor of HCV NS3 protease activity comprising:
  - incubating host cells as defined in claim 15 under conditions which cause expression of said inhibitor-resistant protease, in the absence of a candidate second generation inhibitor compound;
  - incubating said host cells as defined in claim 15 under conditions which cause expression of said inhibitor-resistant protease, in the presence of a candidate second generation inhibitor compound; and
  - measuring the replication of said nucleic acid in the presence and absence of said candidate second generation inhibitor compound,

wherein the level of replication of said nucleic acid is proportional to the activity of said expressed protease, and wherein a decrease in activity of said protease in the presence of a candidate inhibitor compound indicates that said compound inhibits the protease.

**18.** A method for identifying potential a second generation inhibitor of HCV NS3 protease activity comprising:

- incubating an inhibitor-resistant NS3 protease mutant as defined in claim 1 in the presence or absence of a candidate second generation inhibitor compound; and
- measuring the protease activity of said inhibitor-resistant NS3 protease in the presence and absence of said candidate second generation inhibitor compound;

wherein a decrease in activity of said protease in the presence of a candidate second generation inhibitor indicates that said compound inhibits said inhibitor-resistant NS3 protease.